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| 10/524,983 | 06/07/2006 | Richard Albang | GRT/4662-339 | 3944 |

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| EXAMINER | |
|---|---|
| SAIDHA, TEKCHAND | |

| ART UNIT | PAPER NUMBER |
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| 1652 | |

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**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/524,983 | ALBANG ET AL. | |
| | Examiner | Art Unit | |
| | Tekchand Saidha | 1652 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *16 June 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1,13-16,21-23 and 25-40* is/are pending in the application.

4a) Of the above claim(s) *1,22 and 23* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *13-16,21 and 25-40* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☒ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *5/20/2005*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

**DETAILED ACTION**

1. Claim amendment filed June 16, 2008 is acknowledged. Claims 1, 13-16, 21-23 & 25-40 are present in this application.

2. ***Election***

Applicant's election with traverse of Group II (claims 13-16 & 25) drawn to isolated lypolytic enzyme (SEQ ID NO: 36) or the enzyme encoded by the nucleic acid sequence of SEQ ID NO: 34 or 35 is acknowledged. Applicants reasons for the traversal being that at least new claims 27-29, 31-33 & 38-39 should be examined together. Applicants further request that claims to fusion protein be examined together. Applicants' arguments are considered and new claims directed to the polypeptide or the fusion protein comprising the elected polypeptide of the elected group will be examined. Applicants' arguments that all claims be examined is not found to persuasive and no reason given why all the claims be examined.

According claims 13-16, 21 and 25-40 are under consideration in this examination.

3. **Claims withdrawn**:

Claims 1, 22 & 23 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

4. ***Priority***

Acknowledgment is made of applicants' claim for priority based on an applications filed in Europe. Acknowledgment is made of applicant's claim for foreign priority based on an applications filed in Europe on 19 August 2002. It is noted, however, that applicant has not filed a certified copies of the foreign applications as required by 35 U.S.C. 119(b).

5. ***Objection***

The attempt to incorporate subject matter into this application by reference to a hyperlink embedded in the specification (for example, pages 14-15) is improper. Incorporation of subject matter into the patent application by reference to a hyperlink and/or other forms of browser-executable code is considered to be an improper

incorporation by reference. See MPEP 608.01 regarding hyperlinks in the specification and 608.01(p), paragraph I regarding incorporation by reference.

Applicant's cooperation is requested in correcting any errors, including hyperlinks which may be present in the specification, of which applicant may become aware of in reviewing the specification.

6. ***Specification***

The specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicant's cooperation is requested in correcting any errors of which applicant may become aware in the specification.

7. ***Claim Objections***

Claims 13 & 15 are objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form.

Claim 13 recites non-elected SEQ ID NO:!! which must be deleted in response to this Office Action. Claim 15 depends from non-elected claim 1. Proper claim dependency is suggested to overcome this objection.

8. ***Claim Rejections - 35 USC § 112*** (first paragraph)

***Enablement Rejection***

Claims 13-16, 21 and 25-40 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an isolated lipase of SEQ ID NO: 36, or an isolated lipase encoding by the nucleic acid sequence of SEQ ID NO: 34 or 35, does not reasonably provide enablement for any lypolytic enzyme or a protein with *no associated function* and having *varying sequence homologies* of 90% or 95% with respect to the to the sequences of SEQ ID NO: 34, 35 or 36 or a *functional equivalent* of SEQ ID NO: 36 or a functional domain of lypolytic enzyme or a isolated lypolytic enzyme obtainable by expressing a polynucleotide which is hybridizable to the nucleotide sequence of SEQ ID NO: 34 or 35; or fusion proteins thereof (claims 13-16, 21 and 25-40). The specification does not enable any person skilled in the art to which it

pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

The scope of the claims does not commensurate with the enablement provided by the disclosure with regard to the extremely large number of polypeptides broadly encompassed by the claims. Since the amino acid sequence of a protein determines its structural and functional properties, predictability of which changes can be tolerated in a protein's amino acid sequence and obtain the desired activity requires a knowledge of and guidance with regard to which amino acids in the protein's sequence, if any, are tolerant of modification and which are conserved (i.e. expectedly intolerant to modification), and detailed knowledge of the ways in which the proteins' structure relates to its function. However, in this case the disclosure is limited to the nucleotide sequences [SEQ ID NO: 34 & 35] and encoded amino acid sequence of SEQ ID NO: 36.

While recombinant and mutagenesis techniques are known, it is not routine in the art to screen for multiple substitutions or multiple modifications, as encompassed by the instant claims, and the positions within a protein's sequence where amino acid modifications can be made with a reasonable expectation of success in obtaining the desired activity/utility are limited in any protein and the result of such modifications is unpredictable. In addition, one skilled in the art would expect any tolerance to modification for a given protein to diminish with each further and additional modification, e.g. multiple substitutions.

The specification does not support the broad scope of the claims which encompass all modifications of protein of SEQ ID NO: 36 and the encoding DNA of SEQ ID NO: 34 or 35 by 5-10%, because the specification does **not** establish: (A) regions of the protein structure which may be modified without effecting lipase enzyme activity; (B) the general tolerance of lipase enzyme to modification and extent of such tolerance; (C) a rational and predictable scheme for modifying any lipase enzyme residues with an expectation of obtaining the desired enzymatic or biological function capable of catalyzing a defined chemical reaction using known substrates; and (D) the

specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful.

With regard to claims 15 & 25-26 directed to a polynucleotide sequence that hybridizes to the disclosed sequences, Applicants have not sufficiently defined the conditions under which the hybridizations are to take place. Nucleic acid hybridization assays are extremely sensitive to the conditions in which they are performed. The buffer composition, pH, temperature, length of time, salt concentrations, quality and source of template nucleic acid, are all variables which determine the reproducibility of a given hybridization experiment. Given the unpredictability of the art and the nature of hybridization experiments in general, it is not sufficient to merely cite hybridization without a clear and explicit recitation of the conditions associated with the hybridization. For example, the definition of stringency as it pertains to hybridization conditions is subject to interpretation and is different from laboratory to laboratory. Therefore, without a clear and explicit recitation of the conditions which were actually used by Applicants in isolating the claimed polynucleotides which hybridize to the disclosed sequences, the skilled artisan would not be able to practice the claimed invention and would not be reasonably apprised of the metes and bounds of the claimed invention. Without such guidance, the experimentation left to those skilled in the art is undue. Including in the claims the exact nature of the hybridization *high stringent* conditions used to isolate the claimed polynucleotides would aid in overcoming this portion of the rejection.

Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims. The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of exact nature of the lipase enzyme and the variants or fusion proteins thereof is unpredictable and the experimentation left to those skilled in the art is improper, extensive and undue. See In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

9. Claims 13-16, 21 and 25-40 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The specification discloses the reduction to practice of one elected species and 12 non-elected species within the claimed genus; specifically, the protein having the amino acid sequence of SEQ ID NO: 36. There are no drawings or structural formulas disclosed of any other protein having the function of lypolytic enzyme. There is no teaching in the specification regarding the 5%-10% structure can be varied while retaining the ability of the protein to function as a lypolytic enzyme. Further, there is no art recognized correlation between any structure (other than SEQ ID NO: 36) and the lypolytic enzyme activity. Consequently there is no information about which amino acids can vary from SEQ ID NO: 36 in the claimed genus and still retain the catalytic activity.

Although the disclosure of SEQ ID NO: 36 combined with the knowledge would put one in possession of proteins that are at least 90% or 95% identical to SEQ ID NO: 3, the level of skill and knowledge in the art is such that one of ordinary skill would not be able to identify without further testing which of those proteins having at least 90% or 95% identity to SEQ ID NO: 36 (if any) or that encoded by DNA having at least 9% or 95% identity to SEQ ID NO: 34 or 35, and having the activity of lypolytic enzyme. Based on the lack of knowledge and predictability in the art, those of ordinary skill in the art would not conclude that Applicant was in possession of the claimed genus of proteins based on the disclosure of the 13 species protein having lypolytic enzyme activities without guidance to specific modifications.

10. ***Claim Rejections - 35 USC § 112*** (second paragraph)

Claims 13-14, 16, 21 and 25-40 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 13 recites the phrase 'functional equivalent thereof'; claims 16, 28, 32, 36 & 39 recite 'functional domain'; claims 14, 25, 27, 31 & 33 recite the phrase 'obtainable'.

The claims are indefinite because it is not clear what the various phrase viz., 'functional equivalent thereof' and 'functional domain' mean. The definition in the specification covers any fragment length that exhibit lypolytic or biological activity – both the activities (lypolytic or biological activity) are vague because biological activity could also include non-enzymatic activities such as immunological activity and lypolytic can include hydrolytic activities other than lipase. The phrase 'obtainable' is a relative term and not definite and may be substituted with 'obtained from'.

The other claims are included in the rejection for failing to correct the defect present in the base claim(s).

11. The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

The following is a quotation of 35 U.S.C. § 103 which forms the basis for all obviousness rejections set forth in this Office action:

> A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.
>
> Subject matter developed by another person, which qualifies as prior art only under subsection (f) or (g) of section 102 of this title, shall not preclude patentability under this section where the subject matter and the claimed invention were, at the time the invention was made, owned by the same person or subject to an obligation of assignment to the same person.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. › 103, the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary.

Applicant is advised of the obligation under 37 C.F.R. § 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of potential 35 U.S.C. § 102(f) or (g) prior art under 35 U.S.C. § 103.

Claims 13-14, 16, 28, 32, 36 & 39 are rejected under 35 U.S.C. § 102(a) as anticipated by or, in the alternative, under 35 U.S.C. § 103 as obvious over Namboodiri et al. (lipids, Vol. 35, No. 5, pages 495-502, 2000; cited PTO-1449) **or** Sugihara et al. (Agric boil. Chem. 52(6):1591-1592, 1988; cited PTO-1449).

Namboodiri et al. teach an extracellular l,3-specific lipase (X) with molecular weight of 35.5 kDa and an isoelectric point of 4.4 from As- pergillus niger has been purified 50-fold to homogeneity as judged by denaturing polyacrylamide gel electrphoresis and slze-exclusion fast- performance liquid chromatography. The native lipase showed optimal activity between temperatures 35 and 5.5°C and pH 5.0 and 6.0.

The applicant's lipase (Y) has the following characteristics: the calculated molecular weight molecular weight of the lipase (Y) was determined to be 34.06 kDa [i.e. 262 amino acids of SEQ ID NO: 36 X 130 (average MW of an amino acid) = 34,060] compared to that obtained by Namboodiri et al. of 35.5 kD, well within the range of experimental error for molecular weight determination.

The two lipases, both from *Aspergillus niger* would therefore be considered the same no matter whether they were isolated from the natural source or were produced recombinantly and that the amino acid sequence shown being the inherent property of the enzyme would therefore be not patentably distinct.

These rejection are being made under 35 U.S.C. § 102(a) and 35 U.S.C. § 103 because it is not possible for the Examiner to physically compare the claimed lipase and the lipase of Namboodiri et al. Applicant bears the burden of providing evidence which distinguishes the claimed enzyme from that disclosed by Namboodiri et al. A preferred means of providing this evidence is for applicant to submit a side-by-side comparison between the enzyme of the prior art and the claimed enzyme which demonstrates any material differences and shows the claimed lipase to be distinct and unobvious in view

of the enzymes of the prior art. *In re Best,* 430 USPQ (CCPA 1977) and *In re Fitzgerald,* 205 USPQ (CCPA 1980).

12. The reference of Sugihara et al. (Agric boil. Chem. 52(6):1591-1592, 1988; cited PTO-1449) also teach a lipase from *Aspergillus niger* that about 35 kDa and appears to be similar to that disclosed by Namboodiri et al. and is therefore used here in a 102/103 rejection for the same reasons as given in paragraph 11.

13. No claim is allowed.

14. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Tekchand Saidha whose telephone number is (571) 272 0940. The examiner can normally be reached on 8.30 am - 5.00 pm. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Nashaat Nashed can be reached on (571) 272 0934. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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